

The rejection under Section 112, 2nd paragraph has been rendered moot by the editorial amendment to claim 8. By way of clarification, claim 10 does indeed claim the "combination" of a formulation *and* a mucosal surface, rather than the combination of two different formulations.

The Section 103(a) rejections of paragraphs 4, 5 and 7 are rendered moot by the above amendment, essentially combining the limitation of claim 2 into claim 1, since none of these rejections were applied against claim 2.

This leaves only the Section 103(a) rejection of paragraph 6, which does apply to claim 2, and which is respectfully traversed. In essence, the Action requires the combination of three different references, unrelated in their own right, and asserts that these references teach individual aspects of the present invention in a manner that would render the present invention obvious in view of their combined teachings. At the outset, the assertion itself is quite improper, (as based solely on hindsight), *and* the references themselves fail entirely to either make or support such a combination. More importantly, the rejection itself fails to appreciate, or therefore assert, one key feature of this invention, namely, the use of the quaternary ammonium salt (such as benzalkonium chloride) to *enhance* the permeation of the inactivated bioactive peptide into the mucosal surface. Of all the references, only Cardinaux is cited as teaching the use of benzalkonium chloride, though it does so only within a "laundry list" of other suitable compounds, and then only for its conventional use as a preservative. Clearly this reference fails to suggest the use of this compound in the manner presently claimed.

Nor is Applicant aware of any other reference that would teach the use of this compound in the manner presently claimed. At its closest, the art appears to teach that a combination of benzalkonium chloride and a cationic surfactant were found to have an enhancing effect in the iontophoresis of enoxacin. See, for instance, Fang, Intl. J. Pharmacol. 180(2):137-149 (1999). Woog et al. (US Patent No. 5,503,827), in turn, describes a process for the production of multi-dose pharmaceutical preparations containing human protein for infusion or injection, and includes benzalkonium chloride among the various preservatives that can be used in this respect. Both references are discussed in Applicant's PCT application corresponding to the present application, and copies of both will be included with the Supplemental Information Disclosure Statement enclosed herewith.

Accordingly, reconsideration of the pending rejection and allowance of the claims as amended above is respectfully requested.

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Respectfully submitted,


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